The burden of allergic diseases in the Indian subcontinent: barriers and challenges

Allergic diseases occur because of a complex interplay between genetic and environmental factors. High-income countries have faced an allergy epidemic during the past 3–4 decades, with nearly one in four children diagnosed with allergic rhinitis, asthma, or eczema. An increasing prevalence of allergic rhinitis and asthma has also been reported in the Indian subcontinent.[1,2] India is the second most populous country (1·35 billion people) in the world and is classified as a lower-middle income country. Nearly 20% of the world's population live in India.

An estimated 300 million people worldwide have asthma, with 37·9 million in India, equal to 55% of the total UK population.[3] The burden of asthma in India exceeds the number of people with HIV infection or tuberculosis. The phase 3 International Study of Asthma and Allergy in Children (ISAAC)[1] reported an overall prevalence of current wheeze of 7% in Indian children aged 6–7 years and aged 13–14 years, with a higher prevalence of up to 10–20% in some areas.[2] Importantly, 50% or more of this cohort had severe uncontrolled asthma.[1] An Indian study reported that prevalence of allergic rhinitis was 11·3% in children aged 6–7 years, and 24·4% in children aged 13–14 years.[2] The ISAAC study[4] reported 2·7% overall prevalence of current eczema among Indian children aged 6–7 years, and 3·6% among Indian children aged 13–14 years. In contrast to the high prevalence of rhinitis, asthma, and eczema, food allergy was low at 0·14% among Indian children aged 6–11 years.[5]

What are the implications of these data from a public and global health viewpoint? Inhaled and intranasal corticosteroids constitute the mainstay therapies in asthma and rhinitis. Allergic rhinitis co-occurs in 60–70% of children with asthma, and optimal management of rhinitis has a positive effect on the long-term clinical management of asthma. However, inhaled and intranasal corticosteroids are unaffordable for patients with low incomes (India's per capita gross domestic product is US$2172), who often resort to suboptimal oral medications. Patients from middle and low socioeconomic groups with severe asthma are also deprived of immunomodulatory biologic therapies such as omalizumab and mepolizumab because these drugs are unaffordable. Clinical management of these patients might be further compromised by knowledge gaps among practitioners, religious beliefs and myths among patients or parents, social stigma of a chronic ailment, and fear of inhalers being habit-forming medicines.[3]

Worldwide, India has one of the highest concentrations of air pollution caused by biomass, fossil fuels, and vehicular exhausts, and the use of mosquito coils and incense and dhoop sticks is an important cause of indoor pollution.[6] Nearly 77% of the Indian population is exposed to $PM_{2·5}$ exceeding the limit of 40 μg/m³ set by National Air Quality Standards in India (the limit set by WHO is <10 μg/m³).[7] Exposure to ambient $PM_{2·5}$ is associated with asthma exacerbations, cardiovascular events, and premature deaths, and is associated with 26·2% of global disability adjusted life years.[7,8]

Within India, there are variations with respect to weather, pollens and fungal spores, insects such as cockroaches, and other living conditions, and meteorological data regarding environmental allergens are sparse.[9] This variation in conditions and absence of data is further complicated by an absence of access to standardised allergen extracts for skin tests in India, making an accurate allergy diagnosis challenging, leading to poor characterisation of disease and generating unreliable epidemiological data.[9] Additionally, standardised allergen-specific immunotherapy (desensitisation treatment) extracts are not generally available in India, making management of moderate–severe allergic rhinitis challenging.

Patient-level risk stratification and characterisation of disease are key to planning therapeutic strategies.[10] Phenotypic clustering based on published evidence[10] generated from high-income countries might not be directly applicable to the Indian population because of environmental confounders, such as air pollution and parasitic infestation. Parasitic infestation is particularly relevant in the context of biomarkers such as peripheral blood eosinophils, serum total IgE, and sputum neutrophils and eosinophils. Environmental confounders are also relevant in the context of

patient selection for treatment with biologics such as omalizumab and mepolizumab.[10]

Provision of self-injectable epinephrine autoinjectors is essential to the long-term management of anaphylaxis because prompt treatment underpins a favourable clinical outcome. These autoinjectors are currently unavailable in India and patients carry predrawn epinephrine in a 1 ml tuberculin syringe for emergency use. This practice is clearly a clinical risk and does not satisfy basic principles of health and safety.

The field of allergy has not gained an independent specialty status in India, and training is sparse and embedded within respiratory medicine. Therefore, there is an urgent need for a strategic, multipronged, multiprofessional, concerted approach to tackle the burden of allergic diseases and improve air quality standards in the Indian subcontinent. Specific focus is needed on education and training for patients and health-care professionals in allergy, improving access to high-quality allergen extracts for immunodiagnostics, and on safe delivery of allergen-specific immunotherapies. Phenotypic characterisation of allergic conditions in the Indian population will be crucial for the development of precision and personalised medicine for allergic diseases. Initiatives driven by the pharmaceutical industry and the involvement of relevant regulatory authorities are urgently needed for making self-injectable epinephrine autoinjectors and essential treatments for rhinitis and asthma accessible at subsidised and affordable prices.

We declare no competing interests.

*Mamidipudi T Krishna, Padukudru Anand Mahesh, Pudupakkam K Vedanthan, Vinay Mehta, Saibal Moitra, Devasahayam Jesudas Christopher
mtkrishna@yahoo.com

Allergy and Immunology Department, University Hospitals Birmingham NHS Foundation Trust, Birmingham B9 5SS, UK (MTK); Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK (MTK); Department of Pulmonary Medicine, Christian Medical College, Vellore, Tamil Nadu, India (DJC) and Indian Chest Society, Nagpur, Maharashtra, India (DJC); Department of Medicine, Division of Allergy and Immunology, The University of Colorado, Aurora, CO, USA (PKV); Department and Respiratory Medicine, JSS Medical College, JSS Academy of Higher Education and Research, Mysore, India (PAM); Allergy, Asthma and Immunology Associates, Lincoln, NE, USA (VM); and Department of Allergy and Immunology, Apollo Gleneagles Hospital, Kolkota, West Bengal, India (SM)

1 Lai CK, Beasley R, Crane J, Foliaki S, Shah J, Weiland S. Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2009; **64:** 476–83.
2 Singh S, Sharma BB, Salvi S, et al. Allergic rhinitis, rhinoconjunctivitis, and eczema: prevalence and associated factors in children. *Clin Respir J* 2018; **12:** 547–56.
3 Global Asthma Network. The global asthma report 2018. http://www.globalasthmareport.org/resources/global_asthma_report_2018.pdf (accessed Jan 22, 2020).
4 Odhiambo JA, Williams HC, Clayton TO, Robertson CF, Asher MI. Global variations in prevalence of eczema symptoms in children from ISAAC phase three. *J Allergy Clin Immunol* 2009; **124:** 1251–58.
5 Li J, Ogorodova LM, Mahesh PA, et al. Comparative study of food allergies in children from China, India, and Russia: the EuroPrevall-INCO Surveys. *J Allergy Clin Immunol Pract* 2019; published online Dec 16. DOI:10.1016/j.jaip.2019.11.042.
6 Poole JA, Barnes CS, Demain JG, et al. Impact of weather and climate change with indoor and outdoor air quality in asthma: a Work Group Report of the AAAAI Environmental Exposure and Respiratory Health Committee. *J Allergy Clin Immunol* 2019; **143:** 1702–10.
7 Balakrishnan K, Dey S, Gupta T, et al. The impact of air pollution on deaths, disease burden, and life expectancy across the states of India: the Global Burden of Disease Study 2017. *Lancet Planet Health* 2019; **3:** e26–39.
8 Rajak R, Chattopadhyay A. Short and long-term exposure to ambient air pollution and impact on health in India: a systematic review. *Int J Environ Health Res* 2019; **9:** 1–25.
9 Bhattacharya K, Sircar G, Dasgupta A, Gupta Bhattacharya S. Spectrum of allergens and allergen biology in India. *Int Arch Allergy Immunol* 2018; **177:** 219–37.
10 Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014; **43:** 343–73.